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# RESEARCH CORRESPONDENCE

## Don't Overlook Digestive Symptoms in Patients With 2019 Novel Coronavirus Disease (COVID-19)

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In late December 2019, a cluster of patients with pneumonia of unknown cause was linked epidemiologically to a seafood and wet animal wholesale market in Wuhan City, China. The causative pathogen subsequently was identified as the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[1] Over the course of the current pandemic, it became apparent that some patients can present with abdominal symptoms without fever or respiratory manifestations, and could be overlooked by health care providers.

We present a case series of hospitalized patients with SARS-CoV-2 infection whose initial symptoms were gastrointestinal.

### Methods

This retrospective study was approved by the Medical Ethical Committee of Zhongnan Hospital of Wuhan University. We evaluated all 1141 cases of 2019 novel coronavirus disease (COVID-19) admitted to Zhongnan Hospital of Wuhan University from January 1, 2020, to February 20, 2020. A diagnosis of COVID-19 pneumonia was based on the COVID-19 Prevention and Control Program (4th edition) published by the National Health Commission of China.[2]

All patients received chest computed tomography (CT) and had throat-swab specimens obtained and maintained in viral-transport media. Reverse-transcription polymerase chain reaction detection reagents were provided by the Center for Disease Control and Prevention, Wuhan, Hubei Province. Laboratory confirmation of COVID-19 was performed both in our hospital and the Center for Disease Control and Prevention laboratory of Hubei Province. Confirmed cases of COVID-19 infection were defined as those with a positive test result from either laboratory.[3]

### Results

Of 1141 confirmed COVID-19 cases, 183 (16%) presented with gastrointestinal symptoms only, and their clinical characteristics are summarized in Table 1. Men slightly outnumbered women, and the most common gastrointestinal symptom was loss of appetite, followed by nausea and vomiting, which occurred in approximately two thirds of cases. Diarrhea and abdominal pain were the presenting symptom in 37% and 25% of patients, respectively.

Laboratory testing showed that mean leukocyte ($2.7 \pm 0.2 \times 10^9$/L) and lymphocyte ($0.53 \pm 0.014 \times 10^9$/L) counts were below normal, and C-reactive protein levels were increased ($18.7 \pm 6.8$ mg/L). Mild increases in serum aminotransferases were noted (aspartate aminotransferase, $65.8 \pm 12.7$ U/L; alanine aminotransferase, $66.4 \pm 13.2$ U/L), but renal function generally was intact.

At the onset of their illness, 175 of 183 (96%) of patients had lung lesions on chest CT, which were unilateral in 61% of cases. The most common CT findings were abnormal lung texture (83%), ground-glass densities (73%), consolidation (27%), and pleural effusion (11%).

The mean time elapsed for confirmation of COVID-19 was 3.5 days from the onset of symptoms. Of the 183 patients, 7 died of progressive respiratory failure, and 176 recovered.

### Discussion

Patients with COVID-19 typically present with fever or a respiratory syndrome. Our case series shows that some patients can present with gastrointestinal symptoms, with a paucity of other manifestations. Such patients could be overlooked, leading to potentially serious consequences to them and their contacts. It is important that clinicians are aware that COVID-19 can present with predominantly gastrointestinal symptoms, and maintain appropriate vigilance and a high index of suspicion.

SARS-CoV-2 can enter angiotensin converting enzyme II (ACE2)-expressing cells. ACE2 is expressed not only in lung alveolar type 2 cell, but also can be found in the

***Abbreviations used in this paper:*** **ACE2, angiotensin converting enzyme II; COVID-19, 2019 novel coronavirus disease; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.**

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upper esophagus, and in stratified epithelial cells and absorptive enterocytes in the ileum and colon.[4] The enteric symptoms of SARS-CoV-2 may be associated with invaded ACE2-expressing enterocytes.[5] These findings suggest that the digestive system, along with the respiratory tract, may be a potential route for SARS-CoV-2 infection, and could explain why some patients present with gastrointestinal symptoms.

Much still needs to be learned about this zoonotic coronavirus that has crossed species to infect human populations,[6] and its spectrum of disease.

**Table 1.** Patients With COVID-19 Infection Presenting With Gastrointestinal Symptoms

| Clinical characteristics/cases (N = 183) | N (%) | *P* value |
|---|---|---|
| Sex | | .032 |
| Male | 102 (56) | |
| Female | 81 (44) | |
| Age, *y* | 53.8 | |
| Epidemiologic history | | .063 |
| Environmental exposure | 94 (51) | |
| Close contact | 99 (54) | |
| Gastrointestinal symptoms | | |
| Nausea | 134 (73) | |
| Vomiting | 119 (65) | |
| Abdominal pain | 45 (25) | |
| Diarrhea | 68 (37) | |
| Loss of appetite | 180 (98) | |
| Both nausea and vomiting | 37 (20) | |
| Both abdominal pain and diarrhea | 16 (9) | |
| All symptoms | 12 (7) | |
| Laboratory characteristics | | |
| Leukocytes, 3.5–9.5 $\times 10^9$/L | 2.7 ± 0.2 | |
| Lymphocytes, 1.1–3.2 $\times 10^9$/L | 0.53 ± 0.014 | |
| C-reactive protein, 0.0–10.0 mg/L | 18.7 ± 6.8 | |
| Aspartate aminotransferase, 15–40 U/L | 65.8 ± 12.7 | |
| Alanine aminotransferase, 9–50 U/L | 66.4 ± 13.2 | |
| Blood urea nitrogen, 2.8–7.6 mmol/L | 6.4 ± 2.5 | |
| Creatinine, 64–104 $\mu$mol/L | 85.7 ± 37.2 | |
| Chest CT findings | 175 | |
| Unilateral | 107 (61) | |
| Bilateral | 68 (39) | |
| Abnormal lung texture | 145 (83) | |
| Ground-glass shadow | 128 (73) | |
| Pulmonary consolidation | 47 (27) | |
| Unilateral pleural effusion | 13 (7) | |
| Bilateral pleural effusion | 7 (4) | |

COVID-19, 2019 novel coronavirus disease; CT, computed tomography.

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**Conflicts of interest**
The authors disclose no conflicts.